

**DRAFT**  
**II. IN THE CLAIMS (MARKED VERSION)**

2. A method of inactivating a viral or microbial agent in a biological source material with a solution comprising the step of contacting the biological source material with a solution comprising an effective amount of an active ingredient, wherein the active ingredient is selected from the group consisting of:  
Dimethyldecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide.
3. The method of claim 2, wherein the solution further comprises glycerol.
4. The method of claim 3, wherein the active ingredient comprises between 0.001 to 10 percent of the solution.
5. The method of claim 4, wherein the glycerol comprises between 0.6 to 6 percent of the solution.
6. The method of claim 5, wherein the glycerol comprises between 0.6 to 6 percent of the solution.
7. The method of claim 2, wherein the active ingredient is dimethyltetradecylamine.
9. The method of claim 2, wherein the agent is a member of the group consisting of:  
bacteria, yeast, fungi, mycoplasma, mammalian cells, other animal cells, viruses, or lipid enveloped viruses such as, Flaviviridae, Retroviridae, Togaviridae, Rhabdoviridae, Herpesviridae, VSV, SFV, HIV, MuLV, BVDV, and CMV.
10. The method of claim 2, wherein the solution further comprises glycerol.
11. The method of Claim 2 further comprising lysing the source material.

**III. REMARKS**

Claims 1 to 9 stand finally rejected under 35 U.S.C. §103(a) as being unpatentable over US Pat. No. 4,481,189 to Prince (the '189 patent) in view of McCutcheon's and

Davis et al. The Examiner responded to Applicant's Response to the Office Action of March 13, 2002 by stating that Applicant's arguments were considered, but not found persuasive. The Examiner contends that the '189 patent teaches a method of inactivating a virus by contacting blood plasma with a composition comprising a non-anionic detergent and an alcohol of formula  $R_2OH$  wherein  $R_3$  can be an alkyl substituted by one or more hydroxyl groups. The Examiner further contends that the '189 patent teaches that the method of its invention is useful in inactivation of other viruses such as a leukovirus. The Examiner further cites two pieces of prior art, the McCutcheon's page to show that AMDA 14 is a non-anionic detergent and Davis et al. to show that MuLV is a leukovirus. Applicants respectfully request reconsideration of the rejection in light of the following response.

Applicant respectfully requests that the Examiner consider the factual foundation for obviousness. It is well settled in the law that an obviousness determination requires a factual analysis and then an application of the law to those facts. Here, the facts are that the combination would not be obvious to one of ordinary skill in the art.

Applicant has cancelled Claims 1 and 8 and presents Claims 2-7 and 9-12 for examination.

**A. Points**

In brief summary of the main points and differences:

(1) The '189 patent discloses a combination of contacting blood with a **contemplated** and enumerated detergent and alcohol and/or ether. Claim 1 of Applicant's invention discloses inactivation of viral contaminants in a biological source material or process intermediate by contacting the biological source material of interest with a solution containing one or more of Dimethyldecylamine, dimethyltridecylamine, dimethylundecylamine,

dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and/or dimethyltridecylamineoxide. There is no requirement for an alcohol and/or an ether in combination.

- (2) The '189 patent **contemplates**, intends, only certain detergents to be used. Dimethyldecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide are not one of the detergents listed.
- (3) The Examiner specifically states that there are differences between Applicant's invention and the prior art. Moreover, the Examiner has supplied no motivation to combine the abstract references.
- (4) The Courts have repeatedly stated that the chemical and biological arts are inherently uncertain.
- (5) One of ordinary skill in the art would not expect Dimethyldecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide to act as a viral inactivator.

#### B. Analysis of Points

A proper analysis of obviousness takes into account the invention as a whole, i.e. knowledge of one of ordinary skill in the art as applied to the invention as a whole, and the nature of the problem to be solved as a whole. *See In re Keller*, 642 F.2d 413, 425 (CCPA 1981). Here, the Examiner has not considered the invention as a whole, but rather in piecemeal using impermissible hindsight.

The factual foundation includes: 1) the scope and content of prior art, 2) the differences between the prior art and the claims at issue, 3) the level of ordinary skill in the art, and 4) any objective evidence of nonobviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). Here, this factual foundation has not been construed properly, thereby rendering improper a finding of obviousness under the application of the law.

To begin, to ascertain the scope and content of the prior art it is necessary to examine “the field of the inventor's endeavor,” *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.*, 758 F.2d 613, 620, 225 USPQ 634, 638 (Fed. Cir. 1985), and “the particular problem with which the inventor was involved,” *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1535, 218 USPQ 871, 876 (Fed. Cir. 1983) (*quoting In re Wood*, 599 F.2d 1032, 1036, 202 USPQ 171, 174 (CCPA 1979)), at the “time the invention was made,” see 35 U.S.C. Section 103(a).

Here, an application of those factors is properly as follows:

1) **(Scope and Content of the Prior Art)** Broadly, the inventor's field of endeavor is the inactivation of viral contaminants in a biological source material or process intermediate. See Summary, page 2, lines 13-15. Likewise and stated differently, the particular problem with which the inventor was involved was the inactivation of viral contaminants in a biological source material or process intermediate. See *Id.*

The '189 patent specifically states in its Abstract that the plasma derivative, substantially free of active hepatitis B or non-A, non-B viruses being characterized by the presence of factor VIII, is sterilized by contact with a detergent, alcohol, or ether,

preferably a mixture of detergent and ether. Accordingly, the '189 patent is related to the inactivation of hepatitis in blood by contacting the blood with a contemplated and enumerated detergent and an alcohol and/or ether. This is not Applicant's invention.

Applicant's invention relates to methods and processes of inactivating viral contaminants in a biological source material or process intermediate comprising contacting the biological source material of interest with a solution containing one or more of dimethyldodecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide. The '189 patent does not disclose any alkylamine compounds. Therefore, taking the invention as a whole, the invention is not obvious.

As the Examiner stated, an obviousness determination requires an investigation of the scope and content of prior art, the differences between the prior art and the claims at issue, the level of ordinary skill in the art, and analysis of any objective evidence of non-obviousness. Stated another way, obviousness is a question of law based on findings of underlying facts relating to the prior art, the skill of the artisan, and objective considerations. See *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966).

Here, the inventor of the '189 patent was concerned with the inactivation of hepatitis in blood plasma. The inventor of the '189 patent gave numerous examples of nonionic (not ionic, or not dependant on a surface active anion for effect) detergents, but not one of them was an alkylamine compound as presented in Applicant's invention. Therefore, the scope and content of the prior art at the time of Applicant's invention does

not include alkylamine compounds, as claimed, for use in inactivating viral contaminants. The Examiner has admitted as much by stating that the '189 patent does not teach or disclose dimethyldodecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide as a nonanionic detergent. As well, the Examiner stated that the '189 patent does not disclose glycerol.

2) **(Differences Between the Prior Art and the Invention)**

To begin, the differences between Applicant's invention and the cited prior art, one only needs to look at the Examiner's statements. The Examiner has stated that the '189 patent does not contain dimethyldodecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide and does not contain glycerol. In fact, the one page of prior art the Examiner has produced with reference to dimethyltetradecylamine is a list and nothing more. The differences are vast. First, the '189 patent discloses and is concerned with a very narrow field of art, namely inactivating hepatitis virus in a blood sample while only denaturing about 50% of the Factor VIII. See the '189 patent, Abstract. The '189 patent discloses that the prior art processes for inactivating hepatitis denatured the Factor VIII and made it unusable. The '189 patent discloses no more.

Every instance of discussion concerning the process of inactivating hepatitis of the '189 patent includes the addition of a detergent, as is defined in Column 5 of the '189

patent, and an alcohol, as is defined in Column 5 of the '189 patent, or a detergent and an ether, as is defined in Column 5 of the '189 patent. Every example, every description speaks to the requirements of these combinations. Applicant's invention specifically claims, in Claim 1, solely the addition of an effective amount of an active ingredient, wherein the active ingredient is selected from the group consisting of dimethyldecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide.

As well, the '189 patent specifically lists *contemplated* examples. Therefore, the invention only contemplates the specific examples listed, otherwise the patentee would not have used such language. An excerpt from the patent is as follows:

**Contemplated** [Emphasis Added] nonionic detergents include those which disperse at the prevailing temperature up to 0.1% by weight fat in an aqueous solution containing 0.1% by weight fat when 1 gram per 100 ml of detergent is introduced therein. In particular there is contemplated detergents which include polyoxyethylene derivatives of fatty acids, partial esters of sorbitol anhydrides, for example, those products known commercially as Tween 80 and Tween 20 nonionic oil soluble water soluble detergent such as that sold commercially under the trademark "Triton X 100". Also contemplated is sodium deoxycholate as well as the "Zwittergents" which are synthetic zwitterionic detergents known as "sulfobetaines" such as N-dodecyl -N,N-dimethyl-2-ammonio-1-ethane sulphonate and its congeners or nonionic detergents such as octyl-beta-D-glucopyranoside.

Other **contemplated** [Emphasis Added] non-ionic detergents are those having about 15 to about 35, preferably about 18 to 33, oxyethylene units in the molecule, especially in the presence of a mercaptan reducing agent, such as, for example, mercaptoethanol, dithiothreitol, dithioerythritol, and dithiooctanoic acid. Suitable nonionic surfactants are oxyethylated alkyl phenols, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene acids, polyoxyethylene alcohols, polyoxyethylene oils and polyoxyethylene oxypropylene fatty acids. Some specific examples are the following:

alkylphenoxypolyethoxy (30) ethanol  
polyoxyethylene (2) sorbitan monolaurate  
polyoxyethylene (20) sorbitan monopalmitate  
polyoxyethylene (20) sorbitan monostearate  
polyoxyethylene (20) sorbitan tristearate  
polyoxyethylene (20) sorbitan monooleate  
polyoxyethylene (20) sorbitan trioleate  
polyoxyethylene (20) palmitate  
polyoxyethylene (20) lauryl ether  
polyoxyethylene (20) cetyl ether  
polyoxyethylene (20) stearyl ether  
polyoxyethylene (20) oleyl ether  
polyoxyethylene (25) hydrogenated castor oil  
polyoxyethylene (25) oxypropylene monostearate.  
(the '189 patent, Col. 5, ll. 15-56).

It is obvious that the patentee did not attempt to include any other species of detergent. The use of the word "contemplate" clearly acts as a limitation and defines the scope of the disclosure. Webster's New World Dictionary, Third College Edition (1991), on page 300, defines contemplate as 1) to look at intently; gaze at; 2) to think about intently, study carefully; 3) to have in mind as a possibility or plan; **intend**. Accordingly, "contemplate" should be construed, in the broadest reasonable terms, as to intend.

It has long been the law that when a patentee uses a claim term throughout the entire patent specification, in a manner consistent with only a single meaning, he has defined that term "by implication." *Vitronics*, 90 F.3d at 1582, 39 USPQ2d at 1577; see also *Hockerson*, 222 F.3d at 955, 55 USPQ2d at 1490. Here, the patentees use of the term "contemplate" throughout the specification as a list of intended detergents will act as a limitation and limit the construction of the permissible detergents to the ones listed and ones very similar.

Therefore, the '189 patent only 'intended' to disclose the limited species enumerated and ones very similar. Applicant discloses the addition of an effective



amount of an active ingredient, wherein the active ingredient is selected from the group consisting of dimethyldecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide. The '189 patent does not disclose an effective amount of an active ingredient, wherein the active ingredient is selected from the group consisting of dimethyldecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide. Accordingly, there is no teaching of Applicant's invention. Moreover, Applicant's disclosure of amine-containing compounds are vastly different from the enumerated detergents in the '189 patent. Therefore, there has been no teaching of Applicant's invention. One of ordinary skill in the art would appreciate that amines have properties different from the disclosed species. See Exhibit A, ¶ 8 and 9.

The amphipathic charged amines and amphipathic charged amine oxides are different from what the '189 patent "contemplates" will function as an inactivation agent for hepatitis. Coupled with the inherent uncertainty of the chemical and biological arts, especially the chemistry of the biological arts, the '189 patent never states that alkylamines function as inactivators. In fact, the '189 patent is limited, as stated by the specification, to a specific list of detergents that are not even remotely similar to amphipathic charged amines and amphipathic charged amine oxides as claimed by Applicant. The Courts have repeatedly stated that the chemical and biological arts are

inherently uncertain. Especially when the invention is the chemistry of biologics. *See Smith v. Bousquet*, 111 F.2d 157 (CCPA 1940) (noting the unpredictability of the chemical world as it relates to biology). Based upon the uncertainty of chemistry as it applies to biological materials, a higher showing is required to show obviousness. *See Cf. Id.* Here, that showing has not been made.

Applications directed to inventions in arts where the results are unpredictable should not be rendered obvious without disclosure of a specie of the claimed compound. *See Cf. In re Sol*, 1938 C.D. 723; 497 O.G. 546. This is because in arts, such as chemistry, it is not obvious from the disclosure of certain species what other species will work. *In re Dreshfield*, 110 F.2d 235, 240 (CCPA 1940). The general rule is that cases involving chemicals and chemical compounds which differ in their properties from that disclosed in a cited reference must appear in the cited prior art reference either by the enumeration of a sufficient number of the members of a group or with specificity to the compound to serve as a valid prior art reference. *Cf. Dreshfield*, 110 F.2d at 240. Here, the '189 patent makes no reference to an alkylamine compound functioning as an inactivating agent. Furthermore, there is no question that polyoxyethylenes, sulfobetaines, and anhydrides, as disclosed in the '189 patent, differ drastically from that claimed in Applicant's invention. Accordingly, the unpredictability of the art field establishes that there is substantially no similarity between Applicant's invention and the '189 patent. The claims at issue in an embodiment are directed towards either an amphipathic charged amine or an amphipathic charged amine oxide. Therefore, following the well-established case law, all the elements are not present in the cited art

and the references may not serve as a §103(a) rejection. *See In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981).

As stated above, (See Summary, page 2, lines 13-15) the particular problem with which the inventor of the instant application was involved was the inactivation of viral contaminants in a biological source material or process intermediate. The Examiner's statement of the problem presumes the solution. The Examiner has cited prior art in an attempt to locate elements of Applicant's invention. There is no suggestions and/or motivation to combine the art cited by the Examiner. The Examiner has cited a table from an apparent index, an article about leukoviruses, and a patent about inactivating hepatitis in blood. Nowhere has the Examiner shown the necessary teachings to make the combination. The Examiner's formulation of the problem confronting the inventor of the instant application was to state that it would have been obvious to use dimethyltetradecylamine and glycerol because the '189 patent discloses a method of inactivating hepatitis virus by contacting blood plasma with a composition comprising a nonanionic detergent and an alcohol of formula R<sub>3</sub>OH. Accordingly, the Examiner has attempted to frame the solution as part of the problem. Framing the solution as the problem is strictly forbidden by the Courts. *See, e.g., In re Antle*, 444 F.2d 1168, 1171-72, 170 USPQ 285, 287-88 (CCPA 1971) (warning against selection of prior art with hindsight). Framing the solution as the problem is not allowed.

There is no room for dispute that the law requires a suggestion to make a combination and/or modification to prior art to arrive at an applicant's invention. *See In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988) (To establish a prima facie case of obviousness, there must be some objective teaching in the prior art or

that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references). Identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. *See id.* Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. *See In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998); *In re Gordon*, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here, there is no suggestion. Here, the Examiner has simply identified elements of Applicant's invention in the prior art without any legal basis.

Furthermore, the Examiner has adopted a broad definition for a detergent. However, a detergent is not well defined in the art. A detergent may be defined as a synthetic cleansing agent resembling soap in the ability to emulsify oil and hold dirt, and containing surfactants which do not precipitate in hard water. A detergent may also contain protease enzymes and whitening agents. See Exhibit A, ¶ 9. As can be seen, the definition of a detergent is far from clear. Therefore, considering the vast definitions of a detergent and the vast species contained, more specificity is required than the mere recitation that a detergent and an alcohol will function to inactivate a virus.

Furthermore, while the Examiner contends that the '189 patent teaches inactivating viruses in general and cites Column 9, lines 43-50 of the '189 patent in support, the patent teaches far less and is very narrow. However, the Examiner neglected to continue reading the excerpt. The '189 patent specifically states that it is useful in the inactivation of other viruses present in **blood**. The '189 patent provides no support for

the Examiner's contention. Therefore, the '189 patent does not teach the general inactivation of viruses as the Examiner contends.

Accordingly, the teachings of the prior art are not Applicant's invention.

3). **(The level of ordinary skill in the art)**

The level of ordinary skill in the art will be a biochemist or chemist with a graduate degree and five years working experience. This assessment is based on the complexity of the art field, the education level of the average researcher, the nature of the problem to be solved, the disclosure from the prior art, and the like.

4) **(Objective indicia of non-obviousness)**

The named inventor of the present application conducted a study that showed unexpected results. The results are reproduced in the accompanying Exhibit A, Declaration of Scot Shepard. The accompanying Declaration illustrates that amine containing detergents can inactivate viral contaminants in a biological source material or process intermediate. Applicant has demonstrated that only certain compounds function as an inactivator, namely a compound selected from the group consisting of dimethyldodecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide. Below is the table from the Declaration. As can be seen, the addition of dimethyltetradecylamine (DMA C14) did inactivate bovine viral diarrhea virus (BVDV) in the treated run.

The results are summarized in Table 1.

Table 1. Titration of BVDV

Sample	BVDV titer (pfu/ml)
Positive control	$1.38 \times 10^8$
Interference control	$9.08 \times 10^7$
Toxicity control	$6.50 \times 10^6$
DMA-C14 treated	$\leq 1.67 \times 10^0$

Virus was not detected in the DMA-C14 treated control. However, due to the limit of detection for the assay, the titer is reported as less than or equal to 1.67 pfu/ml. The difference between the medium control and the limit of detection for the DMA-C14 treated sample is  $6.5 \times 10^6$  pfu/ml. Thus, the DMA-C14 induced inactivation of BVDV is greater than or equal to 6.5 logs. Accordingly, Applicants have produced objective indicia of non-obviousness and respectfully request reconsideration of the rejection.

### C. Summary of Analysis

In summary, the factual evidence cannot establish obviousness. The Examiner has admitted as much by stating the differences without any showing or suggestion to make a modification. Moreover, Claim 1 does not require both a detergent and either an alcohol and/or an ether. Claim 1 of the instant application only claims the addition of an effective amount of an active ingredient, wherein the active ingredient is selected from the group consisting of dimethyldecylamine, dimethyltridecylamine, dimethylundecylamine, dimethyldidecylamine, dimethyltetradecylamine, dimethylhexadecylamine, dimethyldecylamineoxide, dimethylundecylamineoxide, dimethyldidecylamineoxide, dimethyltetradecylamineoxide and dimethyltridecylamineoxide. Therefore, the rejection is improper and Claim 1 is patentable over the cited prior art. Likewise, the instant application claims alkyl amines that are chemically different from the disclosure of the '189 patent and inherently non-

obvious, as established by the case law because of the inherent uncertainty of the chemistry of biology. One of ordinary skill in the art would not expect that an alkylamine could inactivate a virus. Therefore, for the reasons stated above, Applicants respectfully request that the Examiner withdraw the rejection and allow the claims to issue.

## II. CONCLUSION

The application is believed in a condition for allowance and Applicants respectfully request such action. Applicant extends an invitation for the Examiner to call the below undersigned attorney for any assistance in securing allowance of this application. Please charge deposit account number 02-2334 for any required fees.

Date: \_\_\_\_\_

Sincerely,

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